GP 1623

PATENT
ATTORNEY DOCKET NO. 08269/003001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Arnie Helge DEGGERDAL et al. Art Unit: 1623
Serial No.: 08/849,686 Examiner: G. Kunz
Filed : August 21, 1997
Title : ISOLATION OF NUCLEIC ACID

Assistant Commissioner for Patents
Washington, DC 20231

TRANSMITTAL LETTER AND PETITION FOR AUTOMATIC EXTENSION

Correspondence relating to this application is enclosed. The required fees are computed below. Please apply any charges not covered, or any credits, to Deposit Account No. 06-1050.

Total Claims	24	-	24	=	0	$0
Independent	1	-	3	=	0	$0

Applicant hereby petitions under 37 C.F.R. 1.136 for a two month extension of time. $380

TOTAL FEE DUE: $380

A check for $380 is attached.

Respectfully submitted,

Date: October 12, 1999

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RESPONSE

In response to the Examiner's action dated May 12, 1999, please consider the remarks set forth below.

Pending Claims

Claims 1-24 are pending in the application.

The Invention

The application discloses methods for isolating nucleic acids from a sample. The methods use a solid support that includes an organic polymer, and the nucleic acid is bound to the support in the presence of a detergent and in the absence of any chaotropic agent.

35 U.S.C. §102

Claims 1, 2, and 14 have been rejected as anticipated by the 1994 Pharmacia Biotechnology Products catalog. This rejection is respectfully traversed.

The rejection is premised on the belief that the catalog:

> discloses oligo(dT) Cellulose ... for the isolating of mRNA from a cell lysate which certainly can contain any conventional detergent. Oligo(dT) Cellulose is certainly an organic support which can bind mRNA in the presence of detergents. Furthermore, the material can be washed and the nucleic acid eluted with heat which simply denatures the double-stranded nucleic acid. [emphasis added.]

Applicants respectfully remind the examiner that a proper rejection for anticipation requires that the reference teach every aspect of the claimed invention, either explicitly or impliedly. Any feature not directly taught must be inherently present. MPEP 706.02. A rejection of the present claims as anticipated by the 1994 Pharmacia catalog is improper because the catalog fails to teach every aspect of the claimed invention - either explicitly or inherently.

The catalog fails to disclose expressly (i) the presence of a detergent and (ii) the absence of a chaotropic agent. Since these aspects of the claimed invention are not directly taught by the reference, it is proper to consider whether these aspects of the invention are inherently present in the cited reference.

A rejection based on principles of inherent anticipation requires that the claimed matter be necessarily disclosed in the prior art:

> To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. **Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference**, and that it would be so

> recognized by persons of ordinary skill. [See, M.P.E.P. 2131.02, quoting *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991). Emphasis added.]

In the present case, the 1994 Pharmacia Biotechnology Products catalog fails to satisfy the requirements for anticipation based on principles of inherency. The claim limitations of (i) the presence of a detergent and (ii) the absence of a chaotropic agent are not necessarily present in the 1994 Pharmacia Biotechnology Products catalog. The mere assertion in the Office Action that the cell lysate can contain any conventional detergent does not render the presence of a detergent necessarily present. In addition, the Office Action fails even to acknowledge the requirement that the method is carried out in the absence of any chaotropic agent. Thus, there is nothing on the record establishing that the limitation of "the absence of a chaotropic agent" is explicitly or impliedly disclosed in the cited reference. Since the cited art neither expressly nor inherently discloses (i) the presence of a detergent and (ii) the absence of a chaotropic agent, the rejection under 35 U.S.C. §102 should be withdrawn.

35 U.S.C. §103

I.

Claims 1-12 and 14-18 were rejected as unpatentable for obviousness over the 1994 Pharmacia Biotechnology Products catalog. The rejection is predicated on the belief that:

> [t]he Pharmacia Catalog discloses Oligo(dT) Cellulose which is an organic support which <u>can</u> bind nucleic acids in the presence of a detergent, [etc.]. [emphasis added.]

This rejection is respectfully traversed.

Applicants respectfully point out that a rejection for obviousness requires that the prior art teach or suggest <u>all</u> of the claim limitations. MPEP 2142. In the present case, the rejection for obviousness is flawed because the cited catalog fails to disclose or suggest that the claimed method could or should be carried out (i) in the presence of a detergent and (ii) in the absence of a chaotropic agent. The Office Action merely notes that the catalog discloses an organic support which <u>can</u> bind nucleic acids in the presence of a detergent. However, establishing that a reference <u>can</u> be modified as claimed is not sufficient to establish *prima facie* obviousness. As explained in the MPEP:

> the mere fact that references <u>can</u> be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. [MPEP 2143.01.]

Nothing in the 1994 Pharmacia Biotechnology Products catalog suggests the desirability of isolating nucleic acids (i) in the presence of a detergent and (ii) in the absence of a chaotropic agent. Because these claim limitations are suggested only in the present application - not in the prior art - this rejection for obviousness should be withdrawn.

Moreover, Applicants note that, in the Pharmacia method, probes on the surface of the cellulose resin, i.e.,

oligo(dT), are used to recognize and bind to target sequences having a complementary sequence, i.e., mRNA with poly(A) tails. The target molecules are identified and selected by a hybridization-based method that relies upon the identification of specific predefined sequences, leaving those molecules without poly(A) tails in the sample. In the Pharmacia method, sequence-specific binding occurs. In contrast, in the present invention, binding is sequence-independent, and nucleic acid molecules bind non-specifically to the solid support (see page 5, lines 21-22, of the specification). Thus, the 1994 Pharmacia Biotechnology Products catalog discloses nothing about methods of isolating nucleic acid molecules in general, and it discloses only that hybridization can be used to select particular nucleic acid molecule targets.

The Pharmacia method therefore does not overcome the problems recited in the present application, i.e., the need for improved methods of isolation which are quick and simple and which do not require washing steps (see page 5, lines 5-7, and page 11, line 36, through page 12, line 2, of the specification). The present invention is clearly distinct from the disclosure of the 1994 Pharmacia Catalog. If the sequence-independent binding which forms the basis of the isolation technique of the invention were performed in the Pharmacia method, the Pharmacia method would not work. There would be no selection of RNA with poly-A tails, since other nucleic acids also would be captured. The Pharmacia method is not concerned with, nor suggestive of, the claimed method in which sequence-independent binding occurs.

Indeed, hybridization techniques, such as the Pharmacia technique, are routinely preceded by a blocking step to block available sites on the solid support to avoid sequence-independent binding. Thus, the present invention is concerned with a new approach for isolating nucleic acid molecules which would not have been obvious in view of the cited art. Because the cited reference fails to disclose or suggest the claimed method, which is sequence-independent in nature and requires (i) the presence of a detergent and (ii) the absence of a chaotropic agent, the rejection for obviousness should be withdrawn.

II.

Claims 1-24 were rejected as unpatentable for obviousness over Reardon et al., U.S. Patent No. 4,997,932. This rejection is respectfully traversed because the Reardon et al. patent actually teaches away from the claimed invention.

The rejection is based on the belief that the Reardon et al. patent discloses the isolation of RNA or DNA by binding the nucleic acid to an organic support (e.g., an anion exchange resin). The Office Action states that the cell lysate of the Reardon et al. patent contains a TRIS buffer, a chelating agent (EDTA), and a detergent (Triton-X). Applicants respectfully point out that this rejection is nonetheless flawed because the cited art fails to teach or suggest all of the claim limitations. The Reardon et al. patent fails to disclose or suggest that the method should or even could be carried out in the absence of a

chaotropic agent, as required by the claims. Instead, the Reardon et al. patent discloses a method that utilizes 0.5M guanidine HCl to produce the cell lysate that is applied to the column matrix (see, col. 5, line 47, through col. 7, line 57, of the Reardon et al. patent). Since the guanidine HCl used in the Reardon method is a chaotropic agent, the Reardon et al. patent actually teaches away from the claimed invention, which requires the absence of chaotropic agents (see, page 4, lines 22-23, of the present specification, which explains that guanidinium salts are chaotropic agents). Accordingly, this rejection for obviousness should be withdrawn.

35 U.S.C. §112, ¶2

Claims 13 and 19-21 were rejected as indefinite. The rejection is based on the belief that it is unclear whether the solid supports recited in claims 13 and 19-21 are charge neutral or whether they possess an anionic functional group.

This rejection is respectfully traversed, and applicants submit that the metes and bounds of the claims are clear. Nonetheless, for clarification, applicants point out that hydrophobic surfaces and polyurethane, polystyrene and latex are non-ionic. The limitation "latex," recited in claim 21, does not describe the surface properties of the particles, but rather defines a suspension of small polymer particles in aqueous solution. In view of these clarifications, the rejection under 35 U.S.C. §112, ¶2, should be withdrawn, which action is respectfully requested.

CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is requested.

Enclosed is a petition for automatic extension, along with the required fee. Please charge any additional fees, or make any credits, to Deposit Account No. 06-1050, reference no. 08269/003001.

Respectfully submitted,

Date: October 12, 1999

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